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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/769,404	01/26/2001	Theo Wallimann	8932-296	4809

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EXAMINER	
WANG, SHENGJUN	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 01/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/769,404	WALLIMANN ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 20-28* is/are pending in the application.

4a) Of the above claim(s) *4-6,8-12,15-18 and 25-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7,13,14,20-24 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACITON

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 7, 2004 has been entered.

2. Note the claims have been examined insofar as they read on elected invention and species made without traverse in response filed February 4, 2002 and March 28, 2002.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-3, 7, 13, 14, 20-24, 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaddurah-Daouk (US 5,998,457) in view of Meisner (US 4,772,591), Grant et al. (US 5,888,553), Beale (US 5,756,469) and Beale (US 5,716,926).

3. Kaddurah-Daouk teaches a method of treating osteoporosis or osteoarthritis comprising administering therapeutical effective amount of creatine compound, or a pharmaceutical acceptable salt, to patient. See, particularly, the abstract, table 1-2, and claims 1-12.

4. Kaddurah-Daouk does not teach expressly the employment of creatine pyruvate for the treatment, or the particular amount administered, or the method may be employed for promoting

growth and mineralization of bone; improving acceptance and osseous integration of bone; or accelerating healing as claimed in claims 22-24, or the purity as herein required.

5. However, Grant et al. teaches that the excess of cortisol is known to be a cause of osteoporosis, tissue degeneration, and an anabolic composition with anticortisol effect are used to balance effect of cortisol. The anabolic composition comprising creatine. See, column 1, line 52 bridging column 2, line 59, column 5, lines 56-65.and claim 8. Meisner teaches a method for accelerated wound healing or treating degenerative disorders including periodontal disease osteoarthritis, comprising administering a composition comprising creatine to an animal or human. See, particularly, column 1, line 28 bridging column 2, line 45, column 5, lines 3 bridging column 7, line 10. Beale ('469) teaches creatine pyruvate (pyruvyl-creatine) is particularly useful as cortisol antagonist or cortisol blocker for prevent the catabolic activity of cortisol. See column 1, lines 7-18, 54-60; column 3, lines 46-63, and column 5, lines 54-60. Beale ('926) further teaches that pyruvate is known to be useful for treating osteoporosis. See, claim 24. Furthermore, it is noted that none of the cited references require the presence of all of the three compounds excluded herein: dihydrotriazine, dicyano-diamide, and creatinine.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ creatine pyruvate composition, which is essentially free at least one of the three compounds, for treating connective tissue degenerative disorders, including those unrelated to weight gain or weight lose, such as osteoporosis, osteoarthritis or periodontitis, or for accelerating wound healing, promoting growth of connective tissue (cartilage). Note claims 23 and 24 read on the composition comprising creatine pyruvate, since creatine pyruvate is both a creatine salt, and a pyruvate.

A person of ordinary skill in the art would have been motivated to employ creatine pyruvate for treating connective tissue degenerative disorders, including those unrelated to weight gain or weight lose, such as osteoporosis, osteoarthritis or periodontitis, or for accelerating wound healing, promoting growth of connective tissue (cartilage) because it is prima facie obvious to combine two compounds each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus , the claimed invention which employ a combination (salt) of two compounds known to be useful for treating osteoporosis sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069. Note treating osteoporosis is to promoting minerization of bone. Further, creatine pyruvate is particularly known to be useful for treating disease associated with cortisol activity and connective tissue degenerative disorders is known to be closely related to cortisol activity. Claims 22-24 are obvious because creatine is known to be useful for promoting tissue repair process, and treating osteoarthritis and osteoporosis would also considered as a process of promoting tissue (cartilage) repairing since one of the major symptoms of osteoarthritis and osteoporosis is tissue degeneration. As to claims 28 and 30, note, in view of the teachings of Beale, Meisner and Grant, one of ordinary skill in the art would have appreciated that therapeutic effect of creatine pyruvate is not limited only to the symptoms related to weight gain or weight lose. Claims 13 and 14 are interpretated broadly as read on the elected invention, i.e., no foreign tissue have been introduced into the bond, since human bone are known to contain cells in general and chondrablasts cell particular. Finally, The optimization of a result effective parameter, e.g., the effective amount of creatine, is considered within the skill of the artisan. See,

In re Boesch and Slaney (CCPA) 204 USPQ 215. Furthermore, the instant claims are essentially directed to a particular salt of creatine for treating disorders known to be treated by creatine, or its derivatives, or its salts. Absent evidence to the contrary, the employment of pyruvate creatine is seen to be a selection from amongst equally suitable material and as such obvious. Ex parte Winters 11 USPQ 2nd 1387 (at 1388). As to the negative limitation, "essentially free of one or more of dihydrotriazine, dicyano-diamide, or creatinine," note since the cited references do not teach or suggest the particular requirement of the three compounds, the suggested method would encompass the employment of a composition essentially free of at least one of the compounds. What is claimed herein is a specific range (essentially free) within a broad range (not required). It is well settled that in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

Response to the Argument

Applicants' amendments and remarks submitted July 30, 2004 have been fully considered, but are not persuasive.

6. Applicants argue that the claimed invention is not obvious over the cited prior art because the limitation "essentially free of one or more of dihydrotriazine; dicyano-diamide; or creatinine," because "commercially" available creatine has those compounds as impurity, and Kaddurah-Daouk disclosed that the creatine are "commercially" available. The arguments are not persuasive. None of the cited references teach or suggest that the three compounds are required for the therapeutic purpose. As applicants admitted that those are "impurity" in commercially

available product. Therefore, what is claimed herein is a specific range (essentially free) within a broad range (not required). It is well settled that in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

7. The issue here may be further analyzed by the four-part test set forth in Graham v. John Deer Co. 383 U.S. 1 (1966). The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The prior art suggest the employment of creatine or its salts for treating the disorder; The difference between the prior art and the claims at issue is "essentially free of one or more of dihydrotriazine; dicyano-diamide; or creatinine," the free of these compounds are not critical as to the therapeutical purpose since one or two of these compound may be presence; level of ordinary skill in the art: it is generally acknowledged that it is desirable for the active component in pharmaceutical composition to be as pure as possible, objective evidence present in the application indicating obviousness or nonobviousness: none objective evidence present in the application, only a blank, vague assertion that "commercial" products containing the impurity compounds herein. Base on this analysis, the claimed invention, wherein pure creatine

compound is employed, would have been obvious to one of ordinary skill in the art. It is further noted that claims 23, 24 and 28 do not have the negative limitation.

8. In response to applicant's arguments against the references individually for the rejections of claims 22-24 and 28, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, considering the cited references as a whole, it is known that: creatine compounds are useful for treating osteoporosis or osteoarthritis; excess of cortisol is a cause of osteoporosis, tissue degeneration, and anabolic composition with anticortisol effect are useful for balancing the effect of cortisol; creatine pyruvate is useful for accelerating would healing or for treating degenerative disorders, including osteoarthritis; and creatine pyruvate (the elected compound, a salt of creatine) is a cortisol antagonist. Possessing all the knowledge mentioned above, one of ordinary skill in the art, would have seen the claimed invention, which is drawn to the employment of creatine pyruvate for treating bond or cartilage condition, or for promoting healing of bone disorders, prima facie obvious. The lack of express teaching by Grant that creatine is cortisol antagonist would not weak the over all rejections since Beale disclosed that creatine pyruvate, the elected creatine compound, is a cortisol antagonist.

Applicants further argue that the claimed subject matters, creatine or its salts, or the particular disorder s treated herein are not the preferred embodiment in the cited references, and therefore, the cited references cannot render the claimed invention obvious. The examiner respectfully disagrees. Question under 35 U.S.C. 103 is not merely what reference expressly teach, but what they would have suggested to one of ordinary skill in the art at the time the

invention was made; all disclosures of prior art, including unpreferred embodiments, must considered. In re Lamberti and Konort (CCPA), 192 USPQ 278.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang
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Art Unit 1617